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The importance of re-examination with deep biopsies in diagnosing cervical malignancies despite multiple negative pathology reports: A case report

Maryam Ameri^a, Azadeh Memarian^{a,*}, Nadereh Behtash^b, Mojgan Karimi Zarchi^c

^a Iran University of Medical Sciences, Tehran, Iran

^b Tehran University of Medical Sciences, Tehran, Iran

^c Shahid Sadoughi University of Medical Science, Yazd, Iran

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ABSTRACT

INTRODUCTION: Clinical symptoms of female genital tract lymphoma are often non-specific, and mimic other more common gynecological malignancies. Diagnosis can only be confirmed by histology.

CASE PRESENTATION: We report the case of a 48-year-old multiparous woman who underwent subtotal hysterectomy because of enlarged myomatous uterus and persistent heavy vaginal bleeding. “2 months later”, postoperative pelvic and abdominal CT scan performed because of flank pain, revealed bilateral hydronephrosis. Pelvic and colposcopic exam and cervical biopsy under anesthesia showed benign histology, as reported by two pathologists. Referral to a third pathologist and immunohistochemical (IHC) exam revealed malignant lymphoproliferative disorder.

CONCLUSION: Despite multiple negative pathology reports of the cervical biopsies, bimanual pelvic exam with deep biopsies by a gynecologist, allowed accurate final diagnosis of this unusual case.

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1. Introduction

Primary malignant lymphoma of the female genital tract is rare. Awareness of this rare clinical entity is important because these tumors can present at any age and may mimic squamous cell carcinoma of the cervix clinically. Abnormal uterine bleeding is the most common presenting symptom of primary malignant lymphoma of the cervix. Extent of disease, size of primary lesion and type of lymphoma are significant prognostic features [1].

Because the neoplasm originates in the submucosal cervical stroma and the overlying squamous epithelium is unaffected, cervical smears are usually normal [2].

Twenty-five percent of malignant lymphomas arise at extranodal sites and in only 1 percent of women with extranodal tumors, genital tract is involved [3].

In this rare case we emphasize the role of bimanual pelvic examination with deep biopsies in achieving the final diagnosis of disease in spite of the error of pathology.

2. Case presentation

A 48-year-old multiparous woman (with four normal vaginal deliveries and one cesarean section) was referred to the

gynecology clinic because of enlarged myomatous uterus and persistent heavy vaginal bleeding. She underwent a subtotal hysterectomy and unilateral salpingo-oophorectomy in a hospital in Yazd (Iran). Intraoperatively severe bleeding occurred and dense cervical adhesions to peripheral tissues were found. Pathology report indicated benign leiomyoma. After a few months, an abdomino-pelvic CT scan was performed because of flank pain that revealed bilateral hydronephrosis. The patient was referred to the Gynecology Oncology clinic of Bahman hospital in Tehran. Pelvic and rectovaginal exam and colposcopy were performed. Biopsy report was negative, after which mycobacterium tuberculosis test showed negative results. Under general anesthesia, multiple deep cervical biopsies revealed no malignancy again. The slides were reviewed by another “referral” pathologist who reported atypical lymphoid infiltration, consistent with malignant lymphoproliferative disorder, in parametrial biopsies (Figs. 1). Immunohistochemistry confirmed the diagnosis. The stony appearance of the cervix and a concomitant frozen pelvis strongly supported the diagnosis of cervical malignancy.

3. Discussion

Clinical awareness of this rare possibility is important to achieve early diagnosis and appropriate management. Clinical symptoms of female genital tract lymphoma are often non-specific and mimic other much more common gynecologic pathology. Diagnosis is only confirmed by histology [2].

* Corresponding author. Tel.: +9866551201.

E-mail address: Azade.memarian@gmail.com (A. Memarian).

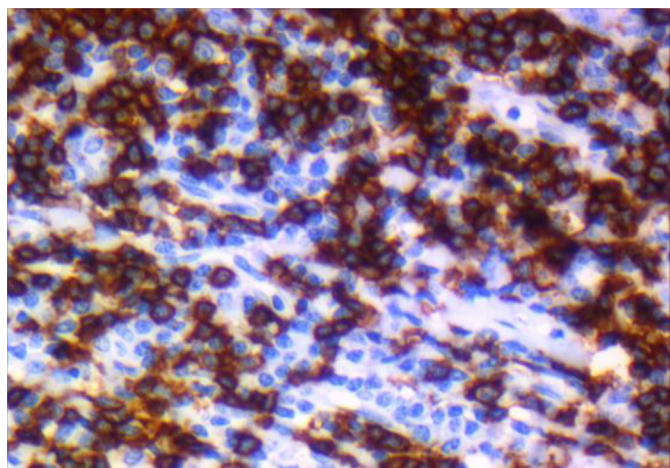


Fig. 1. Histology of the endocervical tumor demonstrated a fairly uniform population of malignant-appearing monomorphic lymphocytes.

The role of deep biopsies in the diagnosis of this rare entity is important.

Diffuse uterine enlargement is the most common appearance. Less commonly, there may be a polypoidal or multinodular mass or a submucosal mass mimicking leiomyoma [4].

Although quite rare, our report should remind the pathologist of considering malignant lymphomas biopsies taken from female genital organ [5], “while reading” deleted.

As these tumors originate within the cervical stroma, the epithelium is initially preserved and therefore, cytology often normal [6]. A deep cervical biopsy is essential for diagnosis [7]. As in this case, multiple surface biopsies were negative, and only the deep biopsies revealed the final diagnosis.

The actual diagnosis may be difficult to reach and usually requires slide review by hematohistopathologists [8].

Primary lymphomas of the uterus or cervix are rare and require an individualized approach to treatment [9].

The findings on cervical cytology in these patients with lymphoma are variable. In most cases the cervical smear is negative, which is probably due to the fact that most lymphomas in this location are subepithelial unless there is ulceration. In some cases, the type of abnormality is misdiagnosed [10].

In each instance, the diagnosis of lymphoma was a morphologic one based on findings from guided or random cervical biopsies. Diagnosis in surgical histopathology is a highly subjective process which is prone to error. The underlying reasons for error in pathology have not been extensively studied. Error can be categorized as being due to a failure to see the feature on the slide (e.g. failing to see an area of malignant cells in a biopsy) or to a failure to correctly diagnose [11].

Reviewing pathology slides before definitive treatment reveals notable discrepancies in diagnoses [12].

Wrong diagnosis by a clinical pathologist could lead to delayed or inappropriate treatment and may result in a legal action from the patient who suffered damages [13].

The role of gynecological examination in the diagnosis of genital cancer is essential. When frozen pelvis and a fixed stony cervix are present, it is necessary to perform multiple deep biopsies in spite of previous negative pathologies. Review of the slides by qualified pathologists can help achieve an accurate diagnosis. Despite histopathological errors, lymphoma should always be considered by pathologists, particularly in these unusual cases.

Conflicts of interest

There is not any conflicts of interest.

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Ethical approval

None.

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